REMARKS

Claims 1-105 are pending. Claims 1-75 have been canceled. Claims 76 and 94 have been amended. New claims 106-142 have been added. Support for the amendment and new claims can be found throughout the specification and claims as filed. In particular, support for the amendment to claims 76 and 94 can be found, for example, on page 9, lines 3-19; page 18, line 28, to page 19, line 12; page 19, line 26, to page 21, line 10; and in Figure 1. Support for new claim 106 can be found, for example, in original claim 76 and on page 13, line 11, to page 14, line 25; page 15, lines 11-23; and page 22, lines 7-11. Support for new claim 121 can be found, for example, in original claim 76, in Figure 1 and on page 18, lines 14-27. Support for new dependent claims 107-111 and 114-118, 120 and 122-127 can be found, for example, in original claims 77-81, 84-86, 90, 92 and 93. Support for new dependent claims 112 and 113 can be found, for example, on page 18, lines 25-27, and in Figure 1. Support for new dependent claim 119 can be found, for example, on page 42, lines 3-9.

Support for new claim 128 can be found, for example, in original claim 94 and on page 13, line 11, to page 14, line 25; page 15, lines 11-23; and page 22, lines 7-11. Support for new dependent claims 129 and 132-136 can be found, for example, in original claims 95, 97-99, 103 and 105. Support for new dependent claims 130 and 131 can be found, for example, on page 18, lines 25-27, and in Figure 1. Support for new dependent claim 137 can be found, for example, on page 42, lines 3-9.

Support for new claims 138-141 can be found, for example, in original claims 94 and 95 and on page 8, line 16, to page 9, line 19; page 18, lines 14-27; and page 22, lines 25-27. Support for new claim 142 can be found, for example, in original claim 94, in Figure 1, and on page 13, line, 22, to page 14, line 4; page 14, lines 15-18; and page 18, lines 25-27. Accordingly, these amendments and new claims do not raise an issue of new matter and entry thereof is respectfully requested. Applicants have set forth the amendment to the claims in clean form above and in Appendix A, with marked up amendments indicated with brackets and underlining. It is respectfully submitted that all of new claims 106-141 are readable upon the elected species.

Regarding Subject Matter Indicated to be Allowable

Applicants appreciate the Examiner's indication that a claim drawn to the structure shown in Figure 1 would be allowable. Applicants bring to the Examiner's attention that new claims 121 and 138-142 are directed to claims reciting the compound of Figure 1. Applicants point out that the leucine tag is recited to be an isotope tag, which refers to a chemical group that can be generated in two distinct isotopic forms (page 18, lines 14-27). Applicants have also included new claim 140, which recites that the leucine tag contains deuterium. New claim 142 is directed to a pair of compounds that are differentially isotopically labeled on the leucine tag.

Regarding Change of Inventorship

Pursuant to 37 C.F.R. § 1.48(a)(1), it is respectfully requested to correct inventorship by adding Drs. Beate Rist, George J. Vella, Subhasish Purkayastha, and Sasi Pillai as a co-inventors with Drs. Ruedi Aebersold and Huilin Zhou. As required under 37 C.F.R. § 1.48 (a)(2), a statement by each of Drs. Rist, Vella, Purkayastha and Pillai is submitted herewith indicating that she or he was not named as an inventor through error and without deceptive intention on her or his part. As required under 37 C.F.R. § 1.48 (a)(3), submitted herewith is a Declaration by the actual inventors, Drs. Aebersold, Zhou, Rist, Vella, Purkayastha and Pillai. Also as required under 37 C.F.R. § 1.48(a)(4), submitted herewith is the processing fee set forth in § 1.17(i).

Additionally as required under 37 C.F.R. § 1.48(a)(5), submitted herewith is a statement by the Assignee of the originally named inventors, The Institute for Systems Biology, consenting to the change of inventorship. A statement under 37 C.F.R. § 3.73(b) showing that the application was assigned to The Institute for Systems Biology was previously filed on October 15, 2001, and thus satisfies the requirement under 3.73(b) for the Assignee to take action.

Change in Entity Status

Small entity status was originally established in good faith for the above-identified application based on the inventorship believed to be correct at the time of filing. Later, an error in inventorship was determined and has been requested to be corrected as set forth above. The change of inventorship has resulted in a change in entity status from small to large. Accordingly, submitted herewith is a communication under 35 U.S.C. § 1.28(c)(2) to correct entity status along with the required large entity fees.

Rejection Under 35 U.S.C. § 112, First Paragraph

The rejection of claims 76-86, 90, 92-99, 103 and 105 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement, is respectfully traversed. The Office Action acknowledges enablement for the structure shown in Figure 1. However, the Office Action indicates that the specification does not provide enablement for a composition comprised of a "solid support" coupled to "cleavable functional groups," "tags," and "reactive groups," either coupled or uncoupled to a sample molecule.

With regard to the assertion that the specification is lacking enablement for preparation and use of a variety of configurations, including whether the sample would remain bound to the solid support after cleavage of the cleavable functional group, Applicants submit that the specification provides

sufficient description and guidance to enable the claimed invention. Nevertheless, claims 76 and 94 have been amended to indicate that the cleavable functional group is covalently coupled to the solid support, the tag is covalently coupled to the cleavable functional group, and the reactive group is covalently coupled to the tag. This amendment obviates the assertion in the Office Action of alleged lack of enablement for the tag being directly attached to the solid support and the sample and cleavable functional group separately attached as pendant groups on the tag. The amendment further obviates the assertion of lack of enablement for the transfer of the tag to the sample molecule while the sample molecule remains bound to the solid support.

With regard to the alleged lack of enablement for "cleavable functional groups," "tags," and "reactive groups" other than those depicted in Figure 1, Applicants respectfully submit that the specification provides sufficient description and guidance for the enablement of these groups. In particular, the specification teaches a variety of "cleavable functional groups," for example, on page 15, line 11, to page 17, line 26. The specification additionally teaches a variety of tags, for example, on page 14, line 5, to page 15, line 10. The specification further teaches a variety of reactive groups, for example, on page 17, line 27, to page 18, line 13. Moreover, it is respectfully submitted that one skilled in the art would readily understand how to prepare the claimed composition containing a chemical group in the spatial configuration where the cleavable functional group is covalently coupled to the solid

support, the tag is covalently coupled to the cleavable functional group, and the reactive group is covalently coupled to the tag. Accordingly, it is respectfully submitted that the specification provides sufficient description and guidance to enable the claimed compositions. Therefore, Applicants respectfully request that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 112, Second Paragraph

The rejection of claims 76-86, 90, 92-99, 103 and 105 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite is respectfully traversed. Regarding the rejection of claim 77 for the term "second messenger," Applicants respectfully submit that the meaning of this term was well known to those skilled in the art. As evidence that "second messenger" was well known to those skilled in the art, attached herewith as Exhibit 1 is the definition of "second messenger," taken from the Oxford Dictionary of Biochemistry and Molecular Biology, page 590, A.D. Smith, ed., Oxford University Press, Oxford (2000). Accordingly, it is respectfully submitted that the term "second messenger" is clear and definite. Therefore, Applicants respectfully request that this rejection be withdrawn.

Claims 90 and 103 are alleged in the Office Action to be unclear for the term "characteristic isotope distribution." Applicants respectfully submit that this term is clear and definite. In particular, the specification teaches that a tag can be an element having a characteristic isotope distribution, and is exemplified by chlorine, bromine, or other elements having

a distinguishable isotopic distribution (page 14, lines 19-22). Accordingly, it is respectfully submitted that the meaning of the term "characteristic isotope distribution" is clear and definite. Therefore, Applicants respectfully request that this rejection be withdrawn.

Claims 76-86, 90, 92-99, 103 and 105 are alleged to be indefinite in that it is unclear where the "solid support" ends up after "after transfer of said tag to said sample." Although Applicants believe that the claims are clear and definite, claims 76 and 94 have nevertheless been amended to explicitly recite that the sample molecule is released from the solid support. It is respectfully submitted that it is clear where the solid support ends up after transfer of the tag to the sample. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The rejection of claims 76-86, 90, 92-99, 103 and 105 as allegedly drawn to an improper Markush group is respectfully traversed. The Office Action asserts that the claimed compositions are directed to conjugates comprised of multiple variables recited as a "solid support," a "cleavable functional group," a "tag," and a "reactive group." Applicants respectfully submit that independent claims 76 and 94, which recite these terms, are not written in Markush form and therefore cannot be directed to an improper Markush group. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 102

The rejection of claims 76-78, 82-84, 90 and 92 under 35 U.S.C. § 102(b) as allegedly anticipated by Gygi et al., Nature Biotechnol. 17:994-999 (1999), is respectfully traversed. Applicants respectfully submit that the claimed compositions are novel over Gygi et al.

With regard to the assertion in the Office Action that the reference describes a "cleavable functional group" in that the protein/peptide of the reference can be cleaved by a protease, it is pointed out that such a "cleavable functional group" is not part of the claimed chemical group but rather is part of the sample molecule. The reagent described by Gygi et al. does not contain a cleavable functional group, as in Applicants' claimed compositions.

Furthermore, Gygi et al. does not describe a reagent where the cleavable functional group is covalently coupled to the solid support, the tag is covalently coupled to the cleavable functional group, and the reactive group is covalently coupled to the tag. Gygi et al. describes derivatization of a protein-containing sample mixture in solution, not the claimed composition, which is used for solid phase labeling of sample molecules. Gygi et al. describes a reagent that contains an isotopically labeled linker and a thiol-specific reactive group, with the linker attached to a biotin affinity tag. Gygi et al. does not describe a reagent where the cleavable functional group is covalently coupled to the solid support, the tag is covalently

coupled to the cleavable functional group, and the reactive group is covalently coupled to the tag. In fact, no where does Gygi et al. describe a reagent with a cleavable functional group or covalent attachment of the reagent to a solid support. Absent such a teaching, Gygi et al. cannot anticipate the claimed compositions. Accordingly, Applicants respectfully submit that the claimed compositions are novel over Gygi et al. and respectfully request that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 103

The rejection of claims 79-81 under 35 U.S.C. § 103 as allegedly obvious over Gygi et al., *supra*, is respectfully traversed. Applicants submit that the claimed compositions are unobvious over Gygi et al.

As discussed above, Gygi et al. does not teach or suggest Applicants' claimed compositions. In particular, Gygi et al. does not teach or suggest a composition containing a chemical group where a cleavable functional group is covalently coupled to a solid support, a tag is covalently coupled to the cleavable functional group, and a reactive group is covalently coupled to the tag. Absent such a teaching or suggestion, Gygi et al. cannot render the claimed compositions obvious. Accordingly, Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned agent or Cathryn Campbell if there are any questions.

Respectfully submitted,

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APPENDIX A

76. (Amended) A composition comprising a solid support coupled to a chemical group comprising a cleavable functional group, a tag and a reactive group covalently linked to a sample molecule, **wherein said cleavable functional group is covalently coupled to said solid support, said tag is covalently coupled to said cleavable functional group, and said reactive group is covalently coupled to said tag and** wherein said cleavable functional group, said tag and said reactive group are positioned relative to each other to allow transfer of said tag to said sample molecule **and release of said sample molecule from said solid support** upon cleavage of said cleavable functional group.

94. (Amended) A composition comprising a solid support covalently coupled to a chemical group comprising a cleavable functional group, a mass spectrometry tag and a reactive group for covalently attaching a sample molecule, **wherein said cleavable functional group is covalently coupled to said solid support, said tag is covalently coupled to said cleavable functional group, and said reactive group is covalently coupled to said tag and** wherein said cleavable functional group, said tag and said reactive group are positioned relative to each other to allow transfer of said tag to **[said] a** sample molecule **attached to said reactive group** upon cleavage of said cleavable functional group **and release of said sample molecule from said solid support**.